Roll out of New TB Regimen in the Philippines: a TB high burden Country

Ma. Tarcela S. Gler, MD

Makati Medical Center

TB Epidemiology Philippines

Metro Manila Population density: 21,765/km2

Stop TB Partnership

TUBERCULOSIS SITUATION IN 2020

PHILIPPINES

Population: 109,581,085
Lower middle-income

591,000 -1% ↓ estimated people who developed TB. Among them 73,000 were Children	334,459 43% ↑ missing people with TB (54,551 were Children)	NA NA estimated people who developed Drug Resistant TB (DR-TB) - a form of TB more difficult to diagnose, treat and cure	NA NA missing people with DR-TB
12,000 0% estimated people who developed TB and were coinfected with HIV	898 -79% ↓ people were diagnosed with both, HIV infection and TB disease	31,000 7% ↑ people died because of TB	TB is the number 2 cause of death among communicable, maternal, neonatal & nutritional diseases

MDR-TB -20% among previously tx and 1.8% among new

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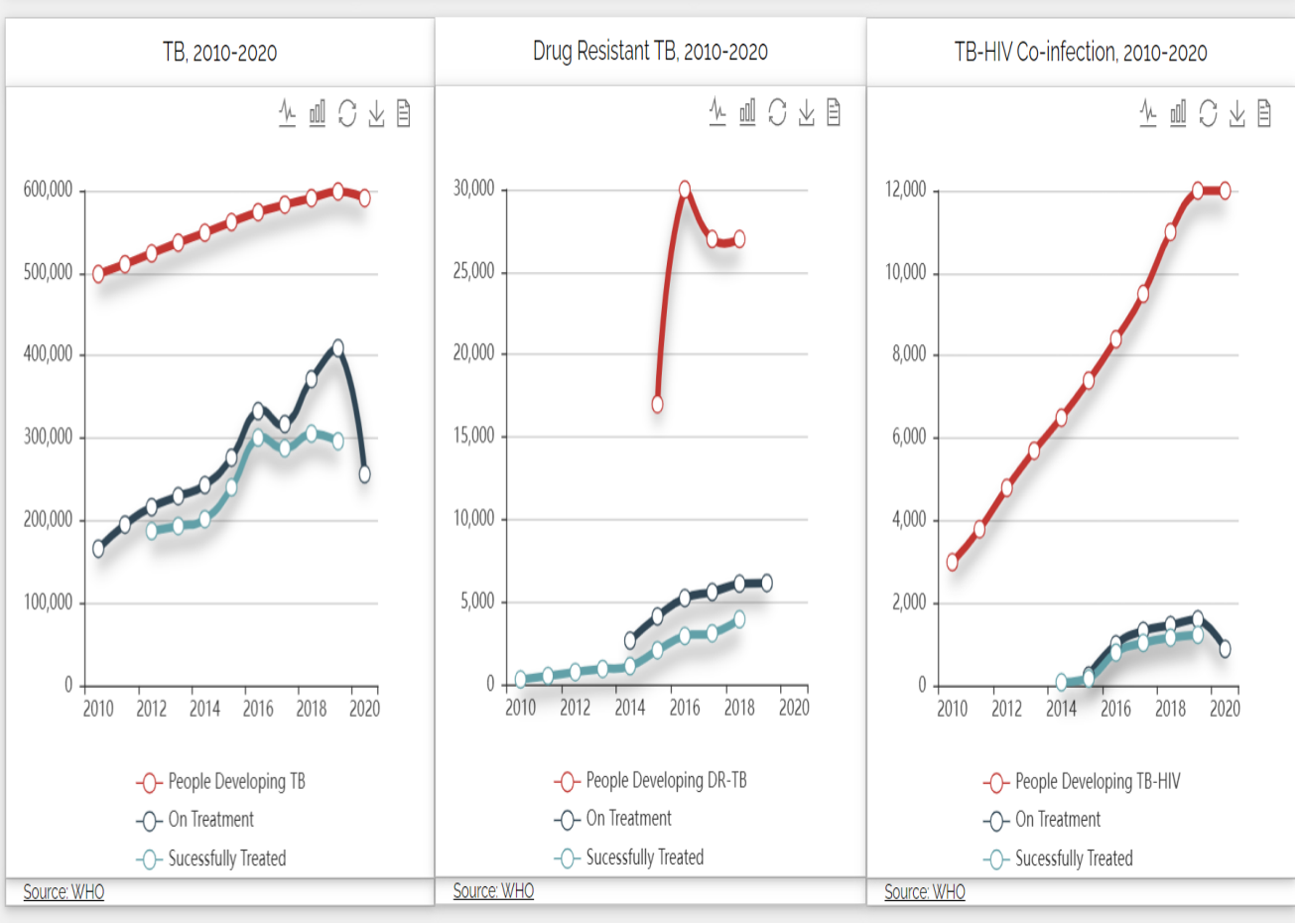
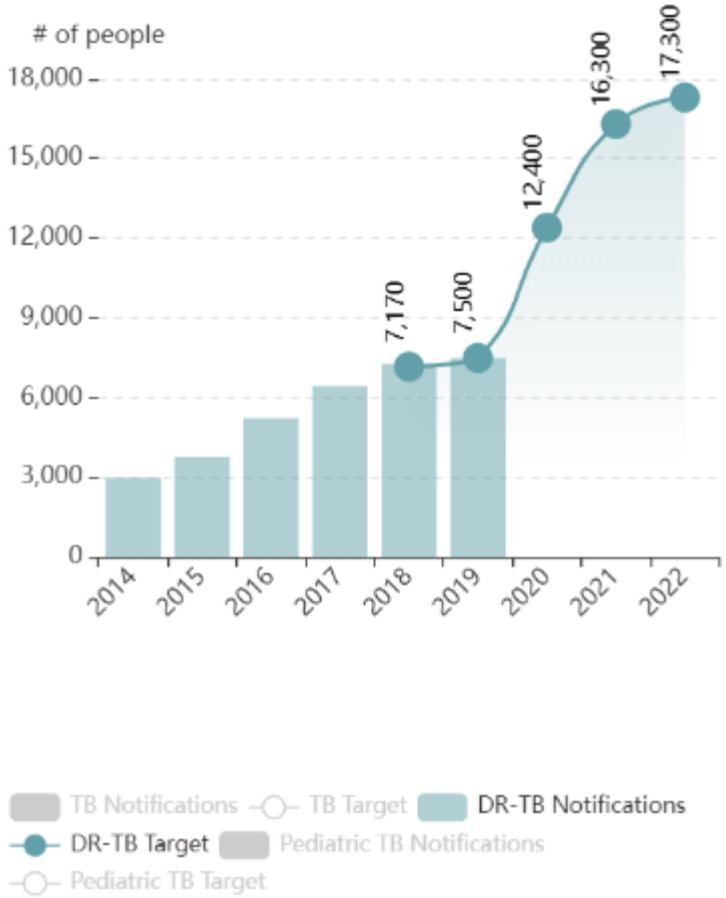




2023 -9800 RR-TB and 7452 initiated on tx (76%); 1022 Gx machines covering 36% of total health facilities

Introduction of New TB Drugs

New TB Drug/Regimen	WHO Guideline	Philippine Guideline	Comments
Programmatic Mgt of DRTB	2006	2014 (MOP 5th ed)	
Standard Shorter Regimen	2016	OR – 2017 Roll-out – 2020 (MOP 6th edition)	Started to roll-out in 2018
Bedaquilline	2013	OR- 2016; roll-out – 2018 Inclusion in MOP - 2020	Increased use during the pandemic
Delamanid	2016	2019	Used sparingly until now
All oral standard short regimen replacing IA with BDQ	2018 (conditional)	Q1 of 2020 thru a Memo in Mar 2020	Patients were put on SAT during the pandemic
6 month all oral regimen (Bpal/BPalM)	2022	OR – 2020 Roll-out Aug 2023	Drugs are still unavailable until now

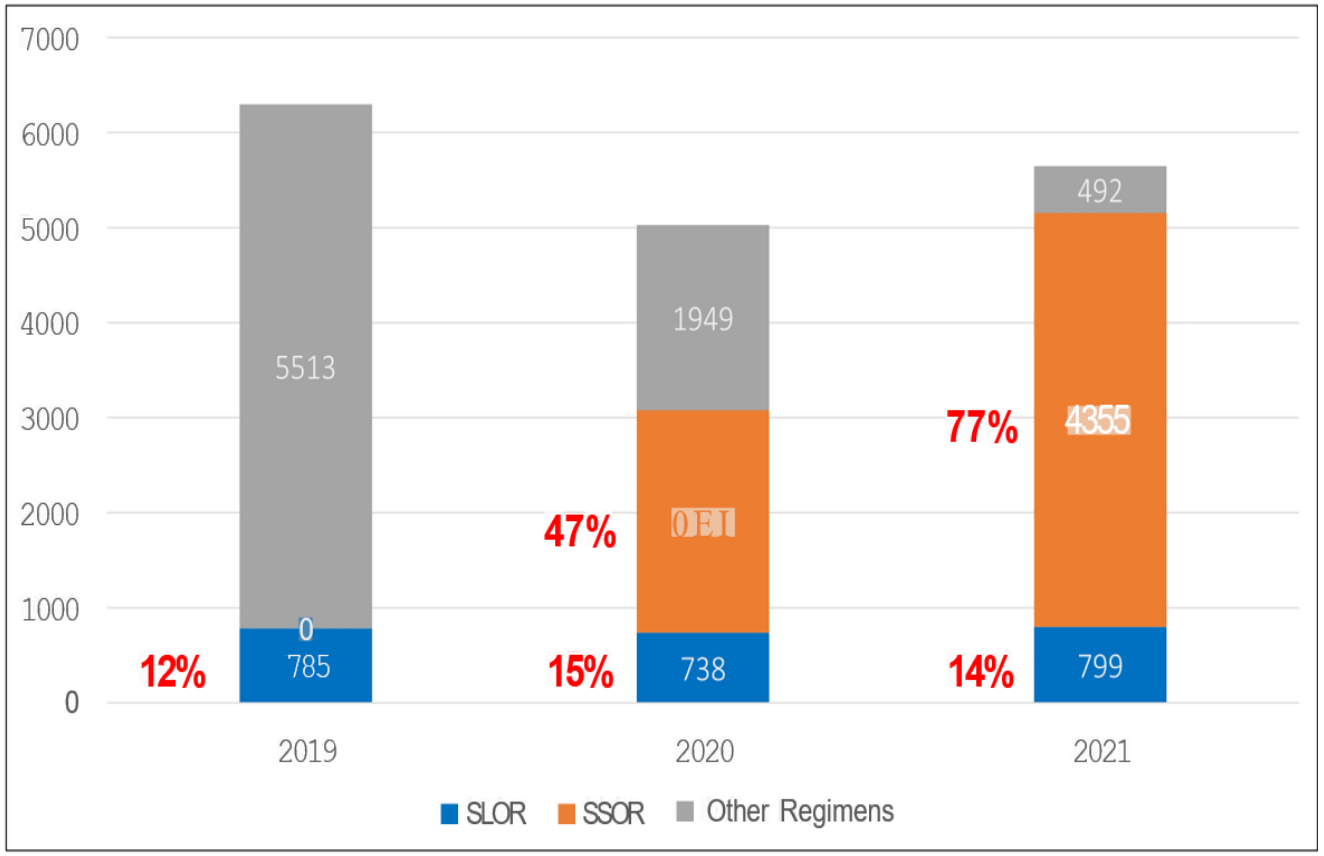
Reasons for delayed roll-out: Operational research prior to roll-out; diagnostics are delayed (delayed lab capacity for LPA) – 2 labs has DST for new drugs (BDQ) ; training of HCW; delayed availability of drugs

Country guideline on use of new/repurposed drugs

Table 18. Type of MDR-TB and RR-TB treatment regimens

Regimen name	Type of DR-TB	Regimen*	Remarks
Regimen 3: Standard Short All Oral Regimen **(SSOR)**	MDR-TB and RR-TB eligible to SSOR	4–6 months: Lfx-Bdq(6)-Cfz-Pto-E-Z-HdH *(Bdq shall always be given for 6 months)* 5 months: Lfx-Cfz-Z-E	
Regimen 4: Standard Long All Oral Regimen for FQ Susceptible **(SLOR FQ-S)**	MDR-TB and RR-TB eligible to SLOR (no FQ resistance)	6 Months: Lfx-Bdq-Lzd-Cfz 12–14 months: Lfx-Lzd-Cfz	Request for "off-label" use at TB MAC if extending use of Bdq beyond 6 months.
Regimen 5: Standard Long All Oral Regimen for FQ Resistance **(SLOR FQ-R)**	MDR-TB and RR-TB eligible to SLOR (with FQ resistance)	6 Months: Lzd-Bdq-Dlm-Cfz-Cs 12–14 months: Lzd-Cfz-Cs	Request for "off- label" use of Bdq and Dlm combination at TB MAC.
Individualized treatment regimen **(ITR)**	Retreatment MDR-TB and RR-TB cases (not eligible to SSOR nor SLOR)	Construct to have at least 4–5 likely effective drugs	Present the case at TB MAC and follow their advice for the regimen design

* Z=Pyrazinamide, E=Ethambutol, Bdq=Bedaquiline, Dlm= Delamanid, Lfx=Levofloxacin, Cfz=Clofazamine, Lzd=Linezolid, Cs=Cycloserine, Pto=Prothionamide, HdH=high dose isoniazid



Note: Treatment start date was used for the cohorting;

TSR 2011-2020: 41-68%; 2019-2022: 68-85%

Potential emergence of drug resistance prior to BDQ/DLM roll-out

- 310 MDR TB isolates (2016 NTPS survey- publicly available data)- Dr Mathema's further interrogation
  - 7 isolates harboring a nsSNP in *pepQ* (M233I, V104M) or *Rv0678* (T161I, D47E, G24S) implicated in Bdq resistance
  - 33 with nsSNP in *ddn* (S132C), *fgd1* (K270M, I162T), *fbiA* (V188F, A178T), *fbiB* (R409C, R265W) or *fbiC* (A855*, G74D, V108A, F744L, R458C, and K141N) implicated in Dlm and Pa resistance
- FQ resistance – NDRS 2014: 0% and 2018:1.5 %; 2019 NTRL routine data – 4.7%; clinic based data- 34%

Phelan; *Sci Rep* 2019
Roa; J Glob Antimicrob Resist 2018

Gaps in the roll out

- Laboratory capacity – only 2 laboratories has capacity DST for any of the new/repurposed drugs available
- No data on BDQ and/or CFz genotypic or phenotypic resistance
- Do periodic drug resistance surveillance (last National DRS was in 2018)
- Training of health care workers on identifying and managing side effects to the new and repurposed agents (the country has incorporated treatment of MDR-TB into the local health centers- HCW in these centers do not have basic knowledge on mech of resistance)
- Very low investment in research locally